	QIE E	1099
	DEC 15 20	RE CE EN
E.	لاد_ ا	A Detitute

Sheet

RADE Dibstitute for form 1449A/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

of

(use as many sheets as necessary)

	Complete if Known	
Application Number	09/308,080	
Filing Date	October 28, 1999	
First Named Inventor	Gonzales, Ph.D., Frank	
Art Unit	1652	_
Examiner Name	Ramirez, Delia M.	
Attorney Docket Number	015280-271100US	

	U.S. PATENT DOCUMENTS+							
/		Document Number		1	Sansa Calumna Linea Wilhord			
Examiner Initials*	Cite No.1	Number Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
				-	8			
					<u> </u>			

				FOREIGN PA	TENT DOCUME	ENTS		
		For	eign Patent Doc	ument		Name of Patentee or	Pages, Columns, Lines, Where Relevant	
Examiner Initials*	Cite No.1	Country Code <sup>3</sup>	Number <sup>4</sup>	Kind Code <sup>®</sup> (# known)	Publication Date MM-DD-YYYY	Applicant of Cited Document	Passages or Relevant Figures Appear	T <sup>6</sup>
2012	1	wo	95/28489		10-26-1995	The UAB Research Foundation		
					_			
								$\Box$
				-			×	
				*				
		1						
	-		<del> </del>					
	<del>                                     </del>	1						

Examiner Signature	Date Considered	3	181	104	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. \*Applicant's unique citation designation number (optional). \*Kind Codes of U.S. Patent Documents at <a href="https://www.uspto.gov">www.uspto.gov</a> or MPEP 901.04. \*Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). \*For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. \*S Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. \*Applicant is to place a check mark here if English language Translation is attached. \*60097522 v1\*\*

DEC 15 2003 Substitute TRADE SUBSTITUTE SUBSTITUTE

Complete if Known fute for form 1449B/PTO Application Number 09/308,080 INFORMATION DISCLOSURE October 28, 1999 Filing Date STATEMENT BY APPLICANT Gonzales, Ph.D., Frank First Named Inventor 1652 Art Unit (use as many sheets as necessary) Ramirez, Delia M. Examiner Name 015280-271100US 2 of Attorney Docket Number Sheet

		NON PATENT LITERATURE DOCUMENTS	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2
on	2	KUILENBURG, Andre B.P. et al.: "Lethal outcome of a patient with a complete dihydropyrimidine dehydrogenase (DPD) deficiency after administration of 5-fluorouracil: frequency of the common IVS14+1G>A mutation causing DPD Deficiency"; Clinical Cancer Research, Vol. 7; pp. 1149-1153; May 2001	
on	3	KUIVANIEMI, Helena et al.: "Identical G+1 to A mutations in three different introns of the Type III procollagene gene (COL3A1) produce different patterns of RNA splicing in three variants ot Ehlers-Danlos Syndrome IV"; J. Biological Chemistry, Vol. 265, No. 20; pp. 12067-12074; July 15, 1990	
M	4	YOKOTA, Hiroshi et al.: "cDNA cloning and chromosome mapping of human dihydropyrimidine dehydrogenase, and enzyme associated with 5-flouorouracli toxicity and congenital thymine uracilura"; J. Biological Chemistry, Vol. 269, No. 37; pp. 23192-23196; September 16, 1994	
on	5	OMIM Entry for "Dyhydropyrimidine Dehydrogenase; DPYD" printed on December 3, 2003; http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=274270; 10 pages	

Examiner Signature	7	Date Considered	3/18/04

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached.

ORIGINALLY FILED

Please type a plus sign (+) inside this box	Please type a plus sign	(+) inside this box	4
---	-------------------------	---------------------	---

PTO/SB/08B (08-00) Approved for use through 10/31/2002 OMB 0851-0031

. . .

Under the Paperwork Reduction Act of 1995, no person Propied to month id to a collection of information unless it contains a valid QMB control number

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT

Compl te If Known **Application Number** 09/308,080 Filing Date October 28, 1999 Frank Gonzalez ECH First Named Inventor **Group Art Unit** 

(use as many sheets as necessary)

Examiner Name Steadman, D

Attorney Docket Number 015280-271100US Sheet of

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the Cite item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue Examiner number(s), publisher, city and/or country where published. No. Initials Gonzalez, F., et al., \*Diagnostic analysis, clinical importance and molecular basis of dihydropyrimidine ΑÇ déhydrogenase deficiency," TIPS, 16:325-327 (1995). Wissen Y. et al. "cDNA cloning and chromosome mapping of human dihydropyrimidine dehydrogenase, an enzyme ΑĎ associated with 5-flourouracil toxicity and congenital thyrnine uraciluria, J. Biol. Chem., 269:23192-23196 (1994). JOURNAL BIOLOGICAL CHEMISTRY, vol. 264, no. 20, July 1990, pages 12067-74, XP002032866 ΑE KUIVANIEMI, H., ET AL: "Identical G to a mutations in three different introns of the type III procellagen gene (COL3A1) produce different patterns of RNA splicing in three variants of Ehlers-Danlos Syndrome IV." ee abstract Meinsma, R., et al., 'Human Polymorphism in Drug Metabolism: Mutation in the Dihydropyrimidine Dehydrogenase Gene Resutls in Exon Skipping and Thymine Uracilurea,' <u>DNA & Cell. Biol.</u>, 14(1)1-8 (1995). NUCLEIC ACIDS RESEARCH. vol. 15 no. 14, 1987, pages 5613-28, XP002032665 AG MARVIT, J. ET AL: "GT to AT transition at a splice donor site causes skipping of the preceeding exon in benylketonuria SINGAPORE JOURNAL OF OBSTETRICS AND GYNECOLOGY. vol. 26, no. 3, November 1995. pages 176-86, XP000600337 ROY ET AL: "molecular scanning of human diseases" see the whole document Vreken, P., et al., "A point mutation in an invariant splice donor site leads to exon skipping in two unrelated Dutch patients with dihydropyrimidine dehydrogenase deficiency." J. Inherit. Metab. Dis., 19(5):645-54 (1996). Wei, X., et al. "Molecular Basis of the Human Dihydropyrimidine Dehydrogenase Deficiency and 5-Fluorouracil Toxicity," J. Clin. Invest., 98(3)610-615 (1996).

Examiner Signature	0-8-	Date Considered	30/02	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231, DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231. WC 9039543 v1

<sup>&</sup>lt;sup>1</sup> Unique citation designation number. <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.